

TOBACCO INDUSTRY RESEARCH COMMITTEE

6. Budget Plan for 1956

350 FIFTH AVENUE

NEW YORK 1, N. Y.

RENEWAL

Salaries
Expendable Supplies
Application For Research Grant
Overhead
Other

20%

5%

30%

10%

5%

#2 R1

Date: September 28, 1955

OK

1. Name of Investigator: Maurice S. Segal, M.D.
Ernst O. Attinger, M.D.

2. Title: Dr. Segal: Clinical Professor of Medicine, Tufts University School of Medicine,
Director, Lung Station (Tufts) and Dept. of Inhalation Therapy,
Boston City Hospital

3. Institution: Dr. Attinger: Research Fellow in Medicine, Tufts Univ. School of Medicine
& Address: Tufts University School of Medicine, 136 Harrison Ave., Boston, Mass.
Boston City Hospital, 818 Harrison Ave., Boston, Mass. Resident in
Lung Station (Tufts) and Dept. of Inhalation Therapy

4. Project or Subject: The Effects of Cigarette Smoking on Normal Subjects

5. Additional Requirements: and Patients with Pulmonary Disease.

This report is available within 4 months and will be available in the form of a book of 20,000 pages.

2. "Respiratory" apparatus for determination of the rate of change in arterial and venous blood. This instrument is currently in the process of construction and will probably be ready for experimental use within 4 months. (Instrument Co., Stamford, Conn.) Its available price is \$1,000.

3. 5. Detailed Plan of Procedure (Use reverse side if additional space is needed): A large number of subjects (especially normals) need to be studied in the manner outlined in the Second Progress Report, (Sept. 1, 1955), in order to determine the nature of the basic changes in respiration and circulation in the lungs with smoking. Some of the factors involved in the changes of compliance and mechanical resistance are the following: change in hydrostatic pressure and changes in intrathoracic blood volume; changes in midposition with change in relative position and dimensions of the tracheobronchial tree, changes in unequal ventilation; changes in surface tension of the lung; and changes in ventilation-perfusion relationships.

To investigate the above which appear to be responsible for the changes noted in the Second Progress Report, the following studies should be carried out in addition to continuing our present studies:

A. Effect of Nicotine by Injection. This study would give some clues to the question if the effects of tobacco upon the mechanics of breathing is a local or a systemic effect.

B. Effect of Nicotine-Free Smoke. This study would help to differentiate between the nicotine effect and the effect of other substances in tobacco upon the mechanics of breathing. *prob. can't elim. nicotine only. describe, ion exch. work*

C. Effect of Tobacco on Pulmonary Circulation. (Catheterization Studies).
A number of investigators have stated that tobacco has an insidious influence on the arteries and on the heart, with a predominant effect on the coronary circulation.

Signature of Project Director
Business Office of the Institution

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Tachycardia, rise in blood pressure and vasoconstriction in the skin have been provoked by the smoking of one cigarette. All three phenomena are usually explained by the nicotine stimulation of the sympathetic ganglia, stimulation of the vasoconstrictor center and the stimulation of the adrenals. The most characteristic quality of nicotine is its influence on the automatic ganglia, which after a short period of stimulation become partially blocked or paralyzed. There is considerable doubt if the pulmonary circulation is subject to reflex mechanism and to the action of drugs which influence peripheral circulation. As the mechanics of breathing are also influenced by the pulmonary blood flow and the intrathoracic blood volume, it seems imperative to study ventilation and circulation at the same time. In order to assure an efficient lung function, an effective gas exchange has to be achieved by a minimal work of breathing and work of the right ventricle. Ventilation might very well improve, while circulation and gas exchange gets worse and vice versa. Therefore catheterization studies including pressure measurements of right auricle, right ventricle and pulmonary pressures, as well as the determination of cardiac output, would be indicated. Furthermore these experiments might shed some light upon the presence or absence of reflexes governing pulmonary circulation.

Our experiments would be conducted as follows in a series of (A) normal subjects and (B) patients. Ventilatory mechanics and hemodynamics would be measured simultaneously under:

- a. Normal breathing.
- b. Induced hypoxia (breathing 14 per cent oxygen)
- c. After smoking one cigarette

D. Effect of unequal ventilation as studied by Rawlert Fowler's single breath technique and by analysis of nitrogen elimination rates over longer periods of time. *injected, I presume. What is previous*
Decrease of compliance with respiratory rate is usually explained on the basis of unequal ventilation. We have certain experimental data, suggesting that this is not *un-esp. immediately* the only factor, but that a change in surface tension brought about by change in *smoking history* intrathoracic blood volume and secretions might also be responsible.

The determination of nitrogen clearance curves by a mass spectrometer offers a relatively simple method to judge the evenness of ventilation at different respiratory rates, and these experiments are of particular interest in view of our findings of the change of compliance with change in respiratory rate in patients with pulmonary disease.

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6. Budget Plan: for 1956

TOBACCO INDUSTRY

350 FIFTH AVENUE

	Salaries	50%	\$11,000.00
	Expendable Supplies	5%	1,100.00
<u>RENEWAL</u>	Applies Permanent Equipment	30%	6,600.00
	Overhead	10%	1,100.00
	Other	5%	1,100.00
	Date: Oct 1955	Total	\$22,000.00

7. Anticipated Duration of Work: Two Years

8. Facilities and Staff Available: Facilities: Dept. of Inhalation Therapy and Lung Station (Tufts) Boston City Hospital; Laboratory and Clinic Facilities, Boston City Hospital; Clinical Facilities
Staff: Maurice S. Segal, M.D., Director, Lung Station (Tufts) and Clinical Professor of Medicine, Tufts University School of Medicine. Ernst O. Attinger, M.D., Research Fellow in Medicine, Tufts University School of Medicine. Dr. Merrill Goldstein, Resident in Medicine, Dept. of Inhalation Therapy, Boston City Hospital. Mrs. D. Belgard, Chief Technician--Scholander, Pulmonary Function Studies, etc. Miss T. Adelman, Assistant Technician--Van Slyke and Pulmonary Function Studies, etc.

9. Additional Requirements:

1. Mass spectrometer (Beckman Model 150), approximately \$5,000. This could be available within 4 months and would be used for continuous analysis of N_2 , O_2 and CO_2 in respiratory gases.

2. "Haemoxymeter" apparatus for determination of partial oxygen tension in arterial and mixed venous blood. This instrument is actually in process of production and will probably be ready for experimental use within some months (Liston-Becker Instrument Co., Stamford, Conn.) No available price as yet.

3. 10. Additional information (including relation of work to other projects and other sources of supply) for at least one ECG machine, \$800.

10. Additional information (including relation of work to other projects and other sources of supply) for at least one ECG machine, \$800. This project is maintained as entirely independent. However, supplemental salary assistance to the technicians and aid for the Assistant Resident in Medicine is supplied through the cooperation of the Trustees of Tufts University School of Medicine and the Boston City Hospital. For further information, please see Second Progress Report of September 1, 1955.

To investigate the above which appear to be responsible for the changes state in the Second Progress Report, the following studies should be carried out in addition to continuing our present activities:

A. Affect of Nicotine on Breathing. This study would give some insight into the question of the effects of tobacco upon the mechanics of breathing is a local or a systemic effect.

B. Affect of Nicotine on Breathing. This study would help to differentiate between the nicotine effect and the effects of other substances in tobacco upon the mechanics of breathing.

Signature: Maurice S. Segal, M.D.

Director of Project

C. Affect of Tobacco on Pulmonary Circulation. (Characterization Studies). Several of investigators have stated that tobacco has an insidious influence on the circulation and on the heart, with a predominant effect on the coronary circulation.

Signature: Joseph M. Hayman, Jr.
Business Officer of the Institution